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A series of spontaneous tumors in mice.

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In the investigation of tumors in mice, attention has been, for the most part, directed to those which develop in the subcutaneous tissue. It is possible that internal tumors often occur unnoticed. In this series the tumors of the lung are most frequent.

Primary, papillary, cyst-adenomata of the lung have been found in eleven cases. All these tumors conform to one type, and consist of cuboidal or columnar epithelium covering irregular folds and processes of connective tissue. No mitotic figures have been found in the epithelium of these tumors, so that it is evident that they are not rapidly growing. Most of these tumors were very minute and in several instances, when they occurred with other primary tumors, they were mistaken for metastases until examined histologically. In one case a tumor of this type attained such size that it filled about one third of the thorax. In two other cases tumors were found growing into the bronchi. These tumors occur in both male and female, and appear to be about equally frequent in the inoculated and non-inoculated mice. The largest of the lung tumors was inoculated into five mice, but failed to develop further.

Minute adenomata of the kidney were found in two cases.

A rapidly growing lympho-sarcoma, which occurred in an old female mouse, was inoculated into seventeen mice with negative results.

Tumors of the mammary gland have developed in three old female mice, and in each case the lymphatics were invaded by the growth. In the first case the primary tumor presents, in addition to simple adenoma, transitions from this to an actively growing carcinoma. Another adeno-carcinoma of the mammary gland occurred in a waltzing mouse. The tumor is peculiar in that groups of the epithelial cells become vacuolated, and resemble very closely the sebaceous glands of the skin. The inoculation

of this tumor into other waltzing mice has been successful in one instance. The growth in this case is relatively slow. A third subcutaneous adeno-carcinoma, differing in structure from both of the preceding ones, has been inoculated into a number of mice, which are now under observation.

Thus in the experimental inoculation of four spontaneous tumors into other mice, a new growth has followed with one only.

An important fact in this series is the relative frequency with which single cases present more than one primary tumor. In three mice there were in each two primary spontaneous tumors of different types. In several other cases a primary tumor occurred in a mouse in which there was also an inoculated tumor.

The mice under observation are kept in small cages, which are kept as clean as possible and scrubbed periodically with hot water and soap. In the seventeen tumors, of this series, there has been no definite indication of cage-infection. On the other hand the frequency of tumors in certain families of mice has suggested the possibility that heredity plays a part in the occurrence of tumors. Certain families of mice, which are susceptible to the inoculable tumors, have developed spontaneous tumors; other families, which are not susceptible to the inoculable tumors, have never developed spontaneous tumors. Since heredity is unquestionably a factor as regards the growth of the inoculable tumors, it should also be considered as a possible factor in the development of spontaneous tumors. Breeding experiments have thus far furnished results in accord with this hypothesis.

Since it has been demonstrated that spirochetæ occur frequently in tumors of mice, silver preparations have been made of several of the tumors of this series, following the technic of Levaditti. No spirochetæ were found in the lympho-sarcoma, but they were found in small numbers in the tumor of the Japanese waltzing mouse. The skin covering this tumor had not ulcerated.

Spirochetæ were also found in the stroma of an inoculated tumor of the Jensen strain. None were found in several human cancers and in an actively growing sarcoma of a hen.

Silver preparations were made of the tissues of several mice which had no tumors. One mouse which had been twice inoculated with the Jensen tumor, died six weeks after the last of the

inoculations. Enormous numbers of spirochetæ, apparently identical with those which occur in the tumors of the mouse, were found in the myocardium and in the lung.

Another mouse, twice inoculated with the Ehrlich "Stamme 11" tumor, died three months after the second inoculation. Neither of the inoculations was followed by any growth of the tumor. There was a long-standing inflammation of one foot and leg. Spirochetæ were found in small numbers about the inflammation in the foot, and in enormous numbers in the mediastinum about the bronchi and large veins. The tubules of the kidney also contain large numbers, but they here appear to be undergoing disintegration and and are not so readily distinguished. The organisms in these two cases are of the form of a relatively thick, broad spiral, and have at one end a flagellum, which is less intensely colored than the body of the organism.

The spirochetæ found in these two cases appear to be identical with those found in the tumors of the mouse.

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Concerning the neutrality of protoplasm.

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It is desirable, both on account of the normal production of acid during metabolism, and because of the production of acid under pathological circumstances, to study the adjustment of equilibrium in protoplasm whereby neutrality is maintained. In undertaking this study the equilibrium in mixtures of sodium hydrate, phosphoric acid and carbonic acid has been studied.

As a result of the investigations it appears that in the presence of both free and combined carbonic acid in measurable amount, such mixtures are precisely neutral to rosolic acid, and that the amount of sodium bicarbonate in such mixtures can vary greatly without great variation in the ratio between mono-sodium phosphate and di-sodium phosphate. These results are in accord with the theory, based upon the ionization constant of carbonic acid